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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/728,355	12/05/2003	Stephen William Watson Michnick	Oddy 004CIP1	2697

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Isaac A. Angres
Suite 301
2001 Jefferson Davis Highway
Arlington, VA 22202

EXAMINER	
LIU, SUE XU	
ART UNIT	**PAPER NUMBER**
1639	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/728,355	WATSON MICHNICK ET AL.	
	Examiner	Art Unit	
	Sue Liu	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,8,11-14,17,20,21,24,30-33 and 37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,8,11-14,17,20,21,24 and 30-33* is/are rejected.

7)☐ Claim(s) *37* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *7/16/07*.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Withdrawal of Finality

1. Upon further consideration, the finality of the previous Office action (mailed 3/12/07) has been withdrawn due to new rejections that are not necessitated by applicant's amendment to the claims.

Claim Status

2. Claims 6, 7, 9, 10, 15, 16, 18, 19, 22, 23, 25-29 and 34-36 have been cancelled as filed on 6/5/07.

Claims 1-5, 8, 11-14, 17, 20, 21, 24, 30-33 and 37 are currently pending.

Claims 1-5, 8, 11-14, 17, 20, 21, 24, 30-33 and 37 are being examined in this application.

Election/Restrictions

3. Applicant's election with traverse of Group I (claims 1-5, 8, 11-14, 17, 20-24, 29-33 and 37) in the reply filed on 5/8/06 is as previously acknowledged.

Priority

4. This application appears to be a CIP of U.S. Patent Application Nos. 09/603,885 (filed 6/26/2000), which is now a US PATENT, 6,897,017 (5/24/2005). The US PATENT, 6,897,017 is a CIP of US Patent Application Nos. 09/017,412 (filed

2/02/1998), which is now a US PATENT, 6,270,964 (8/7/2001). This application also claims priority to U.S. Provisional Patent Application Nos. 60/141,210, filed 6/26/1999.

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 35 U.S.C. 120, 121, or 365(c) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed applications, Application Nos. 09/603,885 and 09/017,412, fail to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application.

The instant application claims methods for identifying an interacting set of molecules using green fluorescent protein or mutants thereof as reporter molecules, which are not methods disclosed by the parent US Application No. 09/603,885 (filed 6/26/2000). The US application 09/603,885 (filed 6/26/2000) only disclosed a method of identifying an interacting set of molecules using DHFR as the reporter enzyme. Therefore, the parent application does not provide support for the instant claimed method of using a fluorescent protein as a reporter molecule.

The '885 application claims priority benefit to the grandparent application (09/017,412,; filed on 2/2/1998; now patented as US 6,270,964), which also does not provide adequate support for the claimed methods of identifying an interacting set of proteins using green fluorescent protein (or broadly using fluorescent protein) or mutants thereof. The only relevant passage in the '412 application is a prophetic discussion of the possibility of using GFP. For example, at cols.23-24 of the '964 patent (parent of the '412 application), the passage recites "Recently the structure of GFP has been solved by two groups, making it now a candidate for a strucutre-based PCA-design *[sic]*, which we have begun to develop" ('964 patent, col.24, lines 13+). That is applicants have not, at the time of filing of the '964 patent, developed the specific structures for the fragmented GFP (or mutants thereof), or fluorescent protein in general that can be reconstituted for the purpose of detecting protein-protein interactions. The recitation of using GFP (or mutants) or fluorescent protein (or mutants) in general in the '964 patent is only prophetic in nature. Thus, as evidenced by cited passage from the parent application ('412), applicants are not in possession of the claimed methods of using GFP or broadly using fluorescent protein in general or mutants thereof.

See Amgen, 927 F.2d at 1206, 18 USPQ2d at 1021 ("it is well established in our law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials, and to describe how to obtain it. Conception does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by its principal biological property ... because an alleged conception having no more specificity

than that is simply a wish to know the identity of any material with that biological property. We hold that when an inventor is unable to envision the detailed constitution of a gene so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, i.e., until after the gene has been isolated.")

Therefore, the instant application would not obtain the priority benefit of the earlier filed applications, 09/603,885 and 09/017,412.

Thus, the effective filing date of the instant application is 12/5/2003.

Claim Rejections Withdrawn

5. Upon further consideration, the following claim rejection is withdrawn:

Claims 1-5, 8, 11-14, 17, 20, 21, 24, 30-33 and 37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

New Claim Objection(s) / Rejection(s)

Claim Objections

6. Claim 37 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claim 37 is not been further treated on the merits.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(Note: the instant claim numbers are in bold font.)

Umezawa WO

8. Claims 1-3, 8, 11-13, 17, 20, 21, 24 and 30-33 are rejected under **35 U.S.C. 102(b)** as being anticipated by Umezawa et al (PCT/JP00/09348; WO 02/08766; 1/31/02; The complete WO document is in Japanese except for the Abstract. The English equivalent, US 20030003506 (a 371 of PCT/JP00/09348) is relied upon for the specific teaching of the WO documents. The relevant citations discussed below correspond to the US 20030003506 document.)

The instant claims recite a method for identifying an interacting set of proteins comprising: A) generating first and second fragments of a fluorescent protein reporter molecule which have a directly fluorescent detectable activity when reconstituted and/or associated, wherein said fluorescent protein is selected from the group consisting of green fluorescent protein and mutants of green fluorescent protein; B) coupling said first fragments of said green fluorescent protein or mutant green fluorescent protein reporter molecule to members of a first panel of proteins; C) coupling said second fragments of said green fluorescent protein or mutant green fluorescent protein reporter molecule to

members of a second panel of proteins; D) mixing the products of B) and C); E) directly testing for fluorescence of said green fluorescent protein or mutant green fluorescent protein reporter molecule when reconstituted and/or associated; and F) identifying the protein panel members whose interaction resulted in fluorescence of said green fluorescent protein or mutant green fluorescent protein reporter molecule and which thus form an interacting set.

Umezawa et al, throughout the publication, teach methods of detecting protein and protein interactions for various proteins (Abstract). The reference teaches splitting a GFP protein into two fragments (e.g. Figure 1; [0020]; [0071]), which read on the generating first and second fragments of GFP of **clms 1-3, 8, 11-13, 17, 20, 21 and 24**.

The reference teaches attaching various proteins such as CaM and M13 proteins (e.g. Example 3), which each of the CaM and M13 protein can be considered as proteins or members of a first or a second panel of proteins according to the definition recited in the instant specification (e.g. p.15, lines 18+). The reference teaching of the specific proteins also read on the step of identifying a first and a second panel of proteins of **clms 2, 8, 12, 21** and **24.**

The reference teaches conjugating various proteins to each of the two fragments (e.g. Figure 1; Figure 4; [0005]; [0008]; [0018]; [0019]; [0020]; [0023]; [0024]; Example 2), which read on method steps B-F of **clms 1-3, 8, 11-13, 17, 20, 21** and **24** because the various proteins attached to the fragments of GFP would be "members of a first (or second) panel of proteins".

The reference teaches detecting the fluorescent signal of the reconstituted GFP (Example 3, especially [0087]), which reads on the optically detectable and fluorescent

signals of **clms 30** and **31**, as well as the inherent property of "generates a signal that can be quantified within living cells" and "can be localized within living cells" recited in **clms 32 and 33**.

Umezawa '506

9. Claims 1-3, 8, 11-13, 17, 20, 21, 24 and 30-33 are rejected under **35 U.S.C. 102(a)** as being anticipated by Umezawa et al (US 20030003506; pub date 1/2/2003).

Umezawa et al, throughout the publication, teach methods of detecting protein and protein interactions for various proteins (Abstract). The reference teaches splitting a GFP protein into two fragments (e.g. Figure 1; [0020]; [0071]), which read on the generating first and second fragments of GFP of **clms 1-3, 8, 11-13, 17, 20, 21 and 24**.

The reference teaches attaching various proteins such as CaM and M13 proteins (e.g. Example 3), which each of the CaM and M13 protein can be considered as proteins or members of a first or a second panel of proteins according to the definition recited in the instant specification (e.g. p.15, lines 18+). The reference teaching of the specific proteins also read on the step of identifying a first and a second panel of proteins of **clms 2, 8, 12, 21** and **24.**

The reference teaches conjugating various proteins to each of the two fragments (e.g. Figure 1; Figure 4; [0005]; [0008]; [0018]; [0019]; [0020]; [0023]; [0024]; Example 2), which read on method steps B-F of **clms 1-3, 8, 11-13, 17, 20, 21** and **24** because the various proteins attached to the fragments of GFP would be "members of a first (or second) panel of proteins".

The reference teaches detecting the fluorescent signal of the reconstituted GFP (Example 3, especially [0087]), which reads on the optically detectable and fluorescent signals of **clms 30** and **31**, as well as the inherent property of "generates a signal that can be quantified within living cells" and "can be localized within living cells" recited in **clms 32 and 33**.

Hamilton '701

10. Claims 1-5, 8, 11-14, 17, 20, 21, 24, and 30-33 are rejected under **35 U.S.C. 102(b)** as being anticipated by Hamilton et al (US 2002/0146701; 10/10/2002).

Hamilton et al, throughout the publication, teach a method of using GFP fragments to detect protein-protein interactions (Abstract). The reference teaches fragmenting GFP (e.g. [0055]+; [0061]; claim 22), which reads on the generating first and second fragments of GFP of **clms 1-3, 8, 11-13, 17, 20, 21 and 24**.

The reference teaches attaching various proteins such as leucine zipper proteins and proteins encoded by cDNA libraries (e.g. [0016]; [0027]; Figure 5; [0066] and [0109] (library of leucine zipper partners)), which read on the step of identifying a first and a second panel of proteins of **clms 2, 8, 12, 21** and **24**. The reference also teaches various libraries of proteins and/or combinatorial libraries as well as screening two libraries (e.g. [0075]+, especially, [0076] and [0078]), which read on the panels of proteins and libraries of proteins of **clms 2, 4, 5, 8, 12, 14, 21** and **24**.

The reference teaches conjugating various proteins to each of the two fragments (e.g. Claim 2; [0109]; Figures 1, [0071]), which read on method steps B-F of **clms 1-3, 8, 11-13, 17, 20, 21** and **24**.

The reference teaches detecting the fluorescent signal of the reconstituted GFP (e.g. [0110]+; Claim 22; Figure 6) and detecting protein interactions using fluorescent cell sorting (i.e. live cells) (e.g. [0071]; [0111]), which reads on the optically detectable and fluorescent signals of **clms 30-33**.

Hamilton '599

11. Claims 1-5, 8, 11-14, 17, 20, 21, 24, and 30-33 are rejected under **35 U.S.C. 102(e)** as being anticipated by Hamilton et al (US 6,780,599; 8/24/2004; filed 5/14/2001; priority date 5/12/2000).

Hamilton et al, throughout the patent, teach a method of using GFP fragments to detect protein-protein interactions (Abstract). The reference teaches fragmenting GFP (e.g. col.9, lines 19+; claim 1), which reads on the generating first and second fragments of GFP of **clms 1-3, 8, 11-13, 17, 20, 21 and 24**.

The reference teaches attaching various proteins such as leucine zipper proteins and proteins encoded by cDNA libraries (e.g. col.3, lines 36+; Figure 5), which read on the step of identifying a first and a second panel of proteins of **clms 2, 8, 12, 21** and **24**. The reference also teaches various libraries of proteins and/or combinatorial libraries as well as screening two libraries (e.g. col.11, lines 54+, especially, col.12, lines 33+), which read on the panels of proteins and libraries of proteins of **clms 2, 4, 5, 8, 12, 14, 21** and **24**.

The reference teaches conjugating various proteins to each of the two fragments (e.g. Claim 1; Figures 1, col.12, lines 33+), which read on method steps B-F of **clms 1-3, 8, 11-13, 17, 20, 21** and **24**.

The reference teaches detecting the fluorescent signal of the reconstituted GFP (e.g. col.17, lines 55+; Claim 1; Figure 6) and detecting protein interactions using fluorescent cell sorting (i.e. live cells) (e.g. col.12, lines 33+); col.17, lines 55+), which reads on the optically detectable and fluorescent signals of **clms 30-33**.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Umezawa WO and Hamilton '701

13. Claims 1-5, 8, 11-14, 17, 20, 21, 24, and 30-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Umezawa et al (PCT/JP00/09348; WO 02/08766; 1/31/02), in view of Hamilton et al (US 2002/0146701; 10/10/2002). (The complete WO document is in Japanese except for the Abstract. The English equivalent, US 20030003506 (a 371 of PCT/JP00/09348) is relied upon for the specific teaching of the said WO document. The relevant citations discussed above correspond to the US 20030003506 document.)

Umezawa et al, throughout the publication, teach methods of detecting protein and protein interactions for various proteins, as discussed above.

Umezawa et al do not explicitly teach the libraries of proteins.

However, Hamilton et al, throughout the publication, teach a method of using GFP fragments to detect protein-protein interactions, as discussed above. The reference

teaches screening protein-protein interaction using various libraries of proteins, as discussed above.

Therefore, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to screen for protein-protein interactions using fragmented GFP fused to libraries of proteins.

A person of ordinary skill in the art would have been motivated at the time of the invention to fuse GFP fragments with libraries of proteins to screen for interactions, because Hamilton et al teach the need to detect protein-protein interactions from libraries of proteins.

A person of ordinary skill in the art would have reasonable expectation of success of achieving such modifications, because the generating protein libraries and fusing library members with GFP fragments are known in the art such as the ones taught by Hamilton et al and Umezawa et al.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Art Unit 1639
8/10/2007

/Jon D. Epperson/
Primary Examiner, AU 1639